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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/006,856	12/06/2001	Kevin` P. Baker	GNE:2830P1C14	8365

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EXAMINER	
MCKELVEY, TERRY ALAN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 03/31/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/006,856	BAKER ET AL.	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-35 and 38-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28-35 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/21/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

JC

DETAILED ACTION

All objections and rejections not repeated in the instant Action have been withdrawn due to applicant's response to the previous Action.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Upon another review of the asserted utilities set forth in the specification, it was determined that the following new rejections are appropriate.

Claim Rejections - 35 USC § 101 and 35 USC § 112, First Paragraph

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-35 and 38-40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to isolated polypeptides comprising SEQ ID NO:194, referred to as PRO1303 in the specification, and polypeptides that have 80% or higher amino acid sequence similarity. The specification does not disclose that PRO1303 has significant homology to other, prior art proteins. The instant specification does not disclose any additional information regarding PRO1303 such as subcellular location, timing of regulation during cellular differentiation, which hormones or transcription factors regulate PRO1303, and what physiological significance is possessed by PRO1303.

The specification also generally asserts that all of the disclosed PRO polypeptides will be useful for a number of purposes; however, none of these asserted uses meet the three-pronged requirement of 35 USC 101 regarding utility, namely, that the asserted utility be credible, specific, and substantial. The asserted utilities will each be addressed in turn.

1. The PRO polypeptide can be used to isolate other polypeptides to which it binds. This asserted utility is not

specific or substantial. Since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1303 polypeptide. Furthermore, since the specification does not disclose how PRO1303 or its binding partners can be used, significant further research would be required of the skilled artisan to identify and reasonably confirm a real world context of use because none are set forth simply by binding another protein.

2. The PRO polypeptide can be used as a molecular marker. This asserted utility is not specific since the same can be done with any polypeptide and thus is not specific to the PRO1303 polypeptide.

3. The PRO polypeptide can be used in tissue typing. The asserted utility is not specific or substantial. With the exception of a few housekeeping genes, all polypeptides have a tissue specific pattern of expression, and thus virtually any polypeptide can be used in tissue typing. Thus, the asserted utility is not specific to PRO1303.

4. The PRO polypeptide can be used in therapy. This asserted utility is not specific or substantial. Since a defect in any polypeptide is likely to cause a disease of some sort, every polypeptide is a target for drug development. Thus, the asserted utility is not specific to the claimed PRO1303

polypeptide. Furthermore, the specification does not disclose a nexus between any specific disease state and a change in amount or form of PRO1303. Significant further research would have to be conducted to identify such a nexus and to thus identify and confirm a real world context of use. Therefore, the asserted utility is not substantial.

5. The PRO polypeptide can be used to identify agonists or antagonists. Since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1303 polypeptide. Furthermore, since no activity has been assigned to PRO1303, the assay cannot be conducted until the specific biological activities of PRO1303 are determined empirically. Therefore, the asserted utility is also not substantial.

The specification also discloses that DNA encoding for PRO1303 tested positive in a gene amplification assay, with the DNA being amplified over 2-fold in primary lung tumors and colon tumors. The utilities asserted based upon this positive result are use as diagnostic markers for determining the presence of tumor cells in lung and/or colon tissue samples and utility in cancer therapy and screening for cancer therapeutics. Even though the DNA encoding PRO1303 has diagnostic utility based upon these results, the PRO1303 polypeptide does not for the following reasons. The increased copy number of DNA does not

provide a readily apparent use for the polypeptide because there is no information regarding level of expression, activity, or role in cancer. Increased copy number of DNA in a cancer or transformed cell does not necessarily result in increased level of expression of the polypeptide, as shown by Konoka et al and Pennica et al. Konopka et al teach that: "Protein expression is not related to amplification of the abl gene but to variation in the level of bcr-abl mRNA produced from a single Ph1 template." (abstract). Pennica et al teach that: "In contrast, WISP-2 mapped to human chromosome 20q12-20q13 and its DNA was amplified, but RNA expression was reduced (2- to >30 fold) in 79% of the tumors." (abstract). These references thus show that even if amplification of a gene occurs in a tumor cell, it does not mean that the mRNA or protein expressed from the gene is also amplified and thus usable as a diagnostic marker for cancer. Since the protein is not necessarily overexpressed in cancer cells, then there is no substantial utility in using the protein for cancer therapy or screening for cancer therapeutics.

A substantial utility, by definition is a utility that defines "real world" use, and a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility. In the instant case, the amplification of

the DNA encoding PRO1303 is, at most, an interesting invitation for further research and confirmation as to whether PRO1303 protein itself is overexpressed or whether high PRO1303 protein expression plays an important role in cancer (and thus might be usable as a therapeutic target). This further research and experimentation, however, is part of the act of invention, and until it has been undertaken, the claimed invention is not considered to have utility based upon gene amplification in tumors.

The specification also discloses that PRO1303 tested positive as stimulators of glucose and/or FFA (free fatty acid) uptake. The asserted utility based upon this assay result is that the polypeptide would be expected to be useful for the therapeutic treatment of disorders where either stimulation or inhibition of glucose uptake by adipocytes would be beneficial for example, obesity, diabetes, or hyper- or hypo-insulinemia. First, the specification does not indicate which asserted utilities correspond specifically to glucose uptake stimulation as opposed to glucose uptake inhibition. Second, the specification does not indicate what, if any of the utilities set forth correspond to stimulation of FFA uptake. Third, the actual assay result is stimulation of glucose and/or FFA uptake, three very different activities (stimulation of glucose uptake

only, stimulation of FFA uptake only, and stimulation of uptake of both). Would PRO1303 polypeptides be useful to treat hyper-insulinemia or would it be useful to treat hypo-insulinemia, two opposite conditions? Fourth, it is unclear how increasing uptake of FFA into adipocytes would treat obesity (or thus diabetes). Fabris et al teaches that in obesity, excessive energy storage as fat is mainly due to an imbalance between energy intake and expenditure, and the preferential channeling of excess calories as fat rather than protein or glycogen may play an important role in the development and maintenance of the disease. FFA-induced insulin resistance saves scarce glucose for central nervous system requirements, but this becomes counterproductive in obesity because it inhibits glucose utilization when there is no need to save it. Glucose and FFA might thus be channeled toward tissues (such as adipose tissue in which insulin sensitivity is maintained or even improved) (page 601, second column). Thus, increase of uptake of FFA and/or glucose into adipocytes does not appear to be a utility for treatment of obesity or diabetes.

Furthermore, the observed differences do not appear to be statistically significant and the cutoff points appear to be arbitrary and there is not obvious scientific basis for them. For example, Santomauro et al. (1999. Diabetes 48:1836-1841)

teach that 56.5% decreases in FFA levels are statistically significant and correlated with physiological improvements, but it is not clear from either the prior art or the specification whether 50% decreases are useful (see Table 2 from Santomauro et al.). Note that 50% decreases in *plasma* insulin do appear to be significant, but it is not clear whether this is due to a doubling of insulin uptake by adipocytes or by other tissues, or whether it is due to changes in the amount of insulin production. Similarly, the observation that 56.5% decreases in *circulating* FFAs is significant and correlated with physiological improvements does not indicate that a doubling of uptake of FFAs *by adipocytes* will lead to the same decreases in FFAs. For example, doubling the amount of FFA uptake from 1% to 2% of total circulating FFAs would not be expected to lead to a 56% decrease in circulating FFA levels.

35 USC § 101 specifically requires that the invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. Because the instant specification, as filed, fails to disclose a specific role of PRO1303 in glucose and/or FFA uptake in adipocytes, one would have reasons to conclude that the instant invention was not completed as filed, and, therefore, clearly lacks utility in currently available form.

A substantial utility, *by definition*, is a utility that defines "real world" use, and a utility that requires or constitutes carrying out further research to identify or reasonably confirm a "real world" context of use is not a substantial utility. In the instant case, the mere fact that the protein encoded by the claimed nucleic acids was "positive" in two assays is at the most, an interesting invitation for further research, experimentation and confirmation as to whether the PRO1303 is useful as a treatment for diabetes, obesity, hyper-insulinemia, or hypo-insulinemia. The further research and experimentation, however, is part of the act of invention, and until it has been undertaken, the claimed invention is not considered specific or substantial.

Claims 28-35 and 38-40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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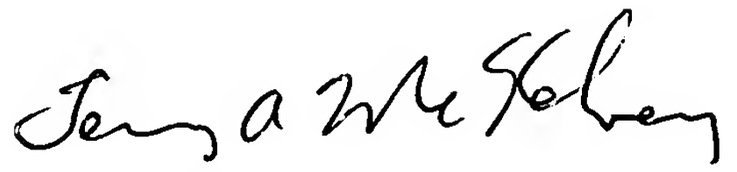
For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (571) 272-0775. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.



Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

March 20, 2005